

EXHIBIT 31

**UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF OHIO
EASTERN DIVISION**

IN RE NATIONAL PRESCRIPTION OPIATE)
LITIGATION)
)
This document relates to:)
) MDL No. 2804
The County of Summit, Ohio, et al. v. Purdue)
Pharma L.P., et al., Case No. 18-op-45090) Hon. Dan Aaron Polster
)
The County of Cuyahoga, Ohio, et al. v. Purdue)
Pharma L.P., et al., Case No. 17-op-45004)
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Expert Report of John Dombrowski, MD
May 10, 2019

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I. Qualifications and Background^{*}

I am a board certified anesthesiologist, with subspecialties in pain and addiction medicine. I graduated with honors from University of Richmond in 1984 with a B.S. in Biology and a minor in Chemistry. I obtained my Master's in Physiology in 1985 from Georgetown University and my medical degree from Georgetown University Medical School in 1989.

Following medical school, I completed my residency training in anesthesiology at Yale University, which included a year of internal medicine and three years in the study of anesthesiology. While at Yale, I received subspecialty training in pain medicine, cardiothoracic anesthesia, and obstetrical anesthesia.

After my studies, I worked as an anesthesiologist in Richmond, Virginia, where I also ran the Acute Pain Service at the Chippenham and Richmond Memorial Hospital. As the Director of Acute Pain Service, I was responsible for managing medication, answering questions from the nursing staff and other hospital staff on appropriate medical care, and giving lectures to the hospital staff.

In 1996, I took a position at Sibley Memorial Hospital in Washington, D.C. as the Director of Pain Medicine. In this position, I cared both for patients with acute pain in the hospital setting and for patients with chronic pain on an outpatient basis. Treatment involved a blend of injection-based therapies and medications.

In 2006, I established the Washington Pain Center, where I have focused on treating chronic pain patients whose pain has not been sufficiently treated by traditional pain medications. In my current medical practice, I care for patients through techniques such as traditional injection therapy, radioablate therapy, prolotherapy, neuromodulation therapy, and intrathecal opioid therapy.

In 2015, I became board certified in addiction medicine. I became Medical Director of three methadone clinics as well as a detoxification facility. Due to my extensive background and training in both addiction and pain management, I have regularly been asked to testify before the U.S. Drug Enforcement Administration ("DEA") and U.S. Food and Drug Administration ("FDA") and to lecture to medical groups.

Recently I have taken a consulting position with the State of Maryland Board of Physicians. In this role, I help educate physicians who have been sanctioned by the Board of Medicine with respect to their prescription writing practices for controlled substances. My goal in this capacity is to educate these physicians on appropriate medication management and other treatment modalities.

I also currently hold a consulting position with the Veterans Administration. In this role, I review medical records concerning the medication management of specific patients in the VA medical system. As with my other consulting, my goal with the VA is to educate physicians, nurse practitioners, and physician's assistants in terms of best practices for the care of our

^{*} I understand that my opinions will be offered on behalf of distributor defendants McKesson Corporation, AmerisourceBergen Drug Corporation, and Cardinal Health, Inc. in this consolidated action.

veterans. At the same time, I work with VA administrators and doctors to identify appropriate or inappropriate opioid medications in order to ensure that the veteran populations are treated appropriately.

A copy of my CV is attached as Exhibit A.

I am being compensated at a rate of \$550 per hour for reviewing medical literature, meetings with counsel, and preparation of an expert report. My rate for providing a full day of testimony at deposition or trial is \$9000. No part of my compensation is contingent upon the outcome of this litigation, and I have no interest in the litigation or with any party.

II. Introduction

In recent years, the media has prolifically covered the opioid crisis facing the United States. The news coverage might convince one that all opioid use in medical treatments is negative, regardless of circumstances. On the contrary, opioid medications provide important therapeutic options for patients with severe acute pain, post-operative pain, cancer-related pain, and chronic pain.

Chronic pain specialists and numerous primary care providers are faced with daily decisions on how best to treat their patients with chronic pain. According to the National Center for Complementary and Integrative Health, a subdivision of the National Institutes of Health, approximately 20 percent of all U.S. adults suffer from chronic pain issues. These issues are particularly prevalent in older Americans, and the number of patients suffering chronic pain is likely to continue to rise as the population ages.¹ Moreover, chronic pain has a deep economic impact as well, with an estimated cost of up to \$635 billion a year.²

With these trends, and given opioids' history in safely and successfully treating pain for many patients, the decision of whether to prescribe opioids is a central part of practitioners' thought processes when treating pain patients. With all the information that is publicly available, both to medical professionals and their patients, this decision of whether and how to prescribe opioid medications for a particular patient can be a challenging one and should not be taken lightly.

Physicians are trained regarding the effects, side effects, benefits, misuse, and risks of medications. Like all medications, opioid medications are neither "all good" nor "all bad." Prescribers continually weigh the risks and the benefits of all medications given to a patient, whether they be blood pressure medicine, anti-seizure medicine, or pain medicine. A central responsibility of a physician is to strike the most effective balance, maximizing positive effects

¹ National Institutes of Health, *Defining the Prevalence of Chronic Pain in the United States* (Sept. 14, 2018), <https://nccih.nih.gov/research/results/spotlight/Prevalence-of-Chronic-Pain>.

² Gaskin DJ, Richard P. The economic costs of pain in the United States. *J Pain*. 2012 Aug;13(8):715-24.

in treating the patient's symptoms or disease while minimizing negative side effects. This continual assessment of the patient is the hallmark of good medical care.

In addition to balancing the potential adverse effects of a medicine with its benefits, physicians also need to consider what therapies are accessible for the patient given constraints like insurance coverage, provider availability, or ease of obtaining treatment. Medication management is often a preferred choice of therapy given these accessibility limitations. In particular, with recent trends in insurance coverage, resources for treatments such as injection-based therapy, physical therapy, work hardening programs, and psychological support are increasingly limited. Often, the only treatment option that insurance carriers will pay for is prescription medications such as opioid medications.

III. Clinical Treatment of Patients with Acute or Chronic Pain

As a clinical physician/anesthesiologist with an extensive background in practicing pain medicine, I review below the approach that physicians like myself generally take when clinically treating a patient with acute and/or chronic pain. In doing so, I place an emphasis on the decisions clinical physicians face and the rationales they deploy when determining the best course of action for such patients. Overall, it is important to understand that prescribing physicians are in a position to treat a patient's pain while minimizing potential risks associated with opioid medications. This is because physicians have the education and experience, as well as access to the specific patient's history, co-morbidities, concomitant medications and other relevant information. Physicians rely on a mixture of their medical training, their review of relevant scientific literature, their clinical experience, and guidance from medical and regulatory bodies in treating pain, including in prescribing opioids. Because prescribing physicians can carefully select patients for whom opioids are prescribed, counsel patients about taking the medication as directed, and monitor patients for aberrant use, these prescribers play the most important role in preventing the development of opioid use disorder, addiction, and overdose.

As in any medical relationship, the treating physician must first obtain the patient's history. The physician must obtain a clear understanding of how long the patient has experienced pain and how the patient's situation has affected his or her life, including daily living, quality of living, ability to work, and ability to function in the home environment. Pain is subjective and has been defined broadly to include not only a physical sensation, but also sensory, emotional, cognitive, developmental, behavioral, spiritual, and cultural components. There are no objective ways to measure pain intensity. Pain, which has been referred to as "the fifth vital sign," is reported by the patient. Accordingly, the physician must pay attention to how the patient describes his or her pain in terms of quality, intensity, and frequency. And although the patient's pain itself is important, the physician also must discern what other aspects of the patient's life have been affected by his or her current condition. This can include a wide range of issues such as sleep disturbances, decreased energy, inability to work, limitations on activities, depression, and anxiety.

As part of the inquiry into the patient's history, the clinical physician must gather information on any tests, studies, surgical procedures, or interventional procedures the patient has undergone in order to assist him or her with his or her current condition. This involves both modalities and therapies that have been beneficial to the patient in the past and interventions that

may not have been as effective. The physician must understand what specific medications (including dosing, frequency of administration, and whether multiple medications were prescribed concomitantly) have been tried in an attempt to alleviate the patient's pain. This is because options for medical management can include changing medications, changing the dose or frequency of existing medication, and/or adding additional medications to emphasize multimodal therapy.

After obtaining an extensive history, the physician typically performs a physical exam. Among other things, the physician usually seeks during the physical exam to gain an understanding of what physical activities trigger the patient's specific pain condition and what activities bring relief for the patient. The physician will also consider laboratory tests, radiology, and other data. All of this information empowers the physician to piece together a potential diagnosis. This diagnosis, in turn, guides the physician to establish a treatment plan.

Obviously, if the specific cause of the patient's pain can be ascertained, this diagnosis will help to guide the physician's treatment decision. In cases in which the root cause of the patient's pain can be effectively treated, the best course of action is to correct the underlying problem. Frequently, however, chronic pain patients do not have a clearly discernable cause of pain that can be treated, and therefore the primary objective of their management becomes effective pain control.

Treatment plans ideally combine several different approaches to pain management and incorporate medication management, procedural therapy, physical therapy, and cognitive behavioral therapy. Unfortunately, the reality is that most patients can only incorporate a smaller selection of these strategies due to time and cost constraints. Moreover, as with pharmacological therapies, other forms of intervention—e.g., physical therapy or neuromodulation—have varying degrees of effectiveness and potential risks such that the best course of action for each patient must be determined individually. Chronic pain is a complex medical condition and as such, there is no single intervention that can be applied across-the-board.

Physicians also often use a multimodal approach to the medication management portion of the treatment plan. Such an approach can encompass a wide range of medications, including anti-seizure medications, common nonsteroidal medications, antidepressant medications, and opioid medications. Clinically, physicians have found that combination therapy tends to be the most beneficial for patients with respect to managing effects and side effects. The goal of combination theory is to use small doses of multiple medications that can work synergistically. Opiate medications are one of the tools that should be considered in this multi-modal approach to pain management.

The physician attempts to ensure that by the end of the evaluation, patients are educated about the full range of treatment options, including an understanding of the possible risks and benefits of each potential therapy option. As part of the informed consent process, patients are actively involved in the decision-making about the course of therapy with which they are most comfortable.

If the physician chooses to prescribe opioids to the patient, after considering factors including abuse potential, he or she may take a range of actions to prevent abuse. One method of

preventing abuse is to require patients to sign an agreement in which they promise to take the medication only as directed, keep it safe and secure, and not sell or share it with others. It is also important to closely monitor patients once they have received a prescription for opioids. The patient's urine can be screened for certain substances routinely and also randomly. The detection of drugs other than the ones prescribed can alert the prescriber that the patient may be at a higher risk for misuse. Similarly, the absence of the prescribed drug may alert the prescriber that patient may be diverting their medications. If a patient appears to be misusing his or her medications, the prescriber should counsel the patient and may ultimately change the patient's treatment.

IV. The History of Opioid Use for Pain

There is a legitimate medical need for opioids to treat pain; this need has long been recognized by the medical community, as well as by federal agencies such as DEA³ and FDA. Opioids are effective treatment for acute pain (e.g., post-surgical pain), cancer pain (e.g., pain related to cancer treatments), and chronic pain. “For many patients, opioid analgesics – when used as recommended by established pain management guidelines -- are the most effective way to treat their pain, and often the only treatment option that provides significant relief.”⁴

Chronic pain—defined as persistent “pain signals” sent to the nervous system for weeks, months, or even years—is, perhaps surprisingly, one of the largest medical challenges facing Americans today. Approximately 20 percent of all U.S. adults experience chronic pain at any given time.⁵ It is estimated that the number of people who suffer from conditions that cause chronic pain outnumber those who have diabetes, heart disease, and cancer—*combined*.⁶ The causes of chronic pain widely vary, and can include common conditions such as cancer, sickle cell disease, arthritis, and other musculoskeletal conditions. The pain itself can manifest in different parts of the body, even for patients with similar diagnoses. This also means that treatments can vary widely between patients, even among those with the same diagnosed cause.

³ *Program Description*, Drug Enforcement Administration Diversion Control Division, https://www.deadiversion.usdoj.gov/prog_dscrpt/index.html (last visited May 10, 2019).

⁴ American Academy of Family Physicians et al., *Promoting Pain Relief and Preventing Abuse of Pain Medications: a Critical Balancing Act* (2001), available at <https://www.deadiversion.usdoj.gov/pubs/advisories/painrelief.pdf>.

⁵ Dahlhamer J, Lucas J, Zelaya C, Nahin R, Mackey S, DeBar L, Kerns R, Von Korff M, Porter L, Helmick C. Prevalence of chronic pain and high-impact chronic pain among adults - United States, 2016. *MMWR Morb Mortal Wkly Rep.* 2018 Sep 14;67(36):1001-1006.

⁶ National Institutes of Health, *Pain Management Fact Sheet* (Oct. 2010), available at [https://report.nih.gov/nihfactsheets/Pdfs/PainManagement\(NINR\).pdf](https://report.nih.gov/nihfactsheets/Pdfs/PainManagement(NINR).pdf).

Opioids⁷ act by binding to specific proteins called opioid receptors that are found both peripherally and centrally, though the central receptors in the spinal cord and brain are most important for controlling pain. These receptors also bind endogenous opioid peptides (endorphins), which are involved in pain modulation and in numerous other functions. These functions include those mediated by the deep structures of the brain—structures involved in reinforcement and reward mechanisms, mood, and stress.⁸

The use of opioid medications in pain management has played a significant role in contemporary medical practice, but opioids have been used in medicine as far back as 4000 BC with the earliest known use of opium for pain relief. In 1803, German chemist Friedrich Serturner isolated morphine, a pure form of opium's active ingredient, and in 1874, a group of scientists synthesized heroin (diacetylmorphine), which was subsequently marketed as more effective and less addictive than morphine. For a time, heroin was legally available as a pill until abusive users started grinding the pills up and inhaling or injecting them.⁹

Our understanding of and medical guidance regarding opioid treatments for pain has evolved over time. The risk of addiction has been known for over a century, and in the 1970s, the use of opioids for chronic pain was discouraged for this reason.¹⁰

⁷ The term “opioid” is used throughout this discussion to refer to all compounds that bind to opiate receptors. “Natural opioids” include alkaloids derived from the opium poppy, such as morphine and codeine. “Semi-synthetic opioids” are drugs synthesized from naturally occurring opiates, such as heroin from morphine and oxycodone from thebaine. “Synthetic opioids” include drugs manufactured in laboratories that have a chemical structure similar to natural opioids, such as methadone and fentanyl. Prescription opioid medications are approved by the FDA for safe and effective treatment of pain. However, like every medication, they can be dangerous when not taken as prescribed.

Though frequently used interchangeably with the term “opioid,” the term “narcotic” is a legal designation rather than a medical one and encompasses a broader range of medication beyond prescription opioids. Thus, this term is not used in this discussion.

⁸ Rosenblum A, Marsch LA, Joseph H, Portenoy RK. Opioids and the treatment of chronic pain: controversies, current status, and future directions. *Exp Clin Psychopharmacol.* 2008 Oct;16(5):405-16.

⁹ Choi CY. Chronic pain and opiate management. *Dis. Mon.* 2016 Sep;62(9):334-45.

¹⁰ Fishbain DA, Cole B, Lewis J, Rosomoff HL, Rosomoff RS. What percentage of chronic nonmalignant pain patients exposed to chronic opioid analgesic therapy develop abuse/addiction and/or aberrant drug-related behaviors? A structured evidence-based review. *Pain Med.* 2008 May-Jun;9(4):444-59.

In the 1980s, two reports published in the peer-reviewed medical literature indicated that opioids could be used for chronic pain with clinical benefit and minimal risk of addiction.¹¹ In 1982, the World Health Organization (WHO) sought to develop a consensus among pain management practitioners, producing a draft set of guidelines and recommendations for prescribing analgesics for chronic pain in cancer patients. These recommendations were initially finalized in 1986 and include a three-step “ladder” for pain treatment that guided doctors to treat patients with “moderately severe pain” with a “weak opioid” like codeine, while patients with “severe pain” were to be treated with morphine.¹² WHO maintains this same ladder today.¹³

After the establishment of the ladder system, physicians began feeling more comfortable with prescribing, and perhaps even morally obligated to prescribe, pain medications for patients with chronic cancer pain. Aggressive treatment for patients experiencing all types of pain became the best practice. For example, in 1990, the president of the American Pain Society published an editorial in the *Annals of Internal Medicine* arguing that the medical profession had not sufficiently improved its practices in assessing and treating pain.¹⁴ He recommended that physicians should work with narcotics control authorities to encourage therapeutic opiate use, noting that “therapeutic use of opiate analgesics rarely results in addiction.”¹⁵ Just over a year later, the American Pain Society promulgated quality assurance standards for relief of acute pain and cancer pain that followed its president’s recommendations: pain was to be charted and displayed; pain intensity should be measured; and sufficiently high levels of reported pain should prompt a reassessment of the pain therapy being provided.¹⁶

In the late 1990s and early 2000s, several independent regulatory bodies provided encouragement and reassurance to physicians with respect to prescribing opioid medications. In 1998, the Federation of State Medical Boards (“FSMB”) made the following observation in its “Model Guidelines for the Use of Controlled Substances for the Treatment of Pain”: “The Board recognizes that controlled substances, including opioid analgesics, may be essential in the treatment of acute pain due to trauma or surgery and chronic pain, whether due to cancer or non-

¹¹ Porter J, Jick H. Addiction rare in patients treated with narcotics. *N Engl J Med.* 1980 Jan 10;302(2):123.; Portenoy RK, Foley KM. Chronic use of opioid analgesics in non-malignant pain: report of 38 cases. *Pain.* 1986 May;25(2):171-86.

¹² See World Health Org., *Cancer Pain Relief* (1986), available at https://apps.who.int/iris/bitstream/handle/10665/43944/9241561009_eng.pdf.

¹³ World Health Org., *WHO’s Cancer Pain Ladder for Adults*, <https://www.who.int/cancer/palliative/painladder/en/> (last visited May 10, 2019).

¹⁴ Max MB. Improving outcomes of analgesic treatment: is education enough? *Ann Intern Med.* 1990 Dec 1;113(11):885-9.

¹⁵ *Id.*

¹⁶ Baker DW, *The Joint Commission’s Pain Standards: Origins and Evolution* (May 5, 2017), available at https://www.jointcommission.org/assets/1/6/Pain_Std_History_Web_Version_05122017.pdf.

cancer origins.”¹⁷ The FSMB also stated: “Pain should be assessed and treated promptly, and the quantity and frequency of doses should be adjusted according to the intensity and duration of the pain. Physicians should recognize that tolerance and physical dependence are normal consequences of sustained use of opioid analgesics and are not synonymous with addiction.”¹⁸

In 2000 the Joint Commission on Accreditation of Healthcare Organizations announced standards for pain management including the use of a quantitative measure of pain on a systematic basis.¹⁹ And in 2004, the FSMB issued revised guidelines for pain treatment with statements that were even stronger than those in the 1998 version, threatening physicians with sanctions for departing from the standard of care if they did not treat pain aggressively enough:

Inappropriate pain treatment may result from physicians’ lack of knowledge about pain management. Fears of investigation or sanction by federal, state and local agencies may also result in inappropriate treatment of pain. Appropriate pain management is the treating physician’s responsibility. As such, the Board will consider the inappropriate treatment of pain to be a departure from standards of practice and will investigate such allegations, recognizing that some types of pain cannot be completely relieved, and taking into account whether the treatment is appropriate for the diagnosis.²⁰

In short, aggressive treatment of pain, including chronic pain, with opioid medications was being advocated by many regulatory and healthcare organizations during this time.

In fact, physicians who “under-prescribed” opioids for the treatment of pain were at times subject to legal actions. Examples include an Oregon physician who was disciplined in 1999 by the Oregon Medical Board for failure to adequately treat his patients for pain and a California physician who was sued successfully in 2001 for inadequately treating a patient’s pain.²¹ These

¹⁷ Federation of State Medical Boards of the U.S., Inc., *Model Guidelines for the Use of Controlled Substances for the Treatment of Pain* (May 1998).

¹⁸ *Id.*

¹⁹ Joint Commission on Accreditation of Healthcare Organizations, *Pain Standards for 2001* (2001), https://www.jointcommission.org/assets/1/6/2001_Pain_Standards.pdf; Baker DW, *The Joint Commission’s Pain Standards: Origins and Evolution* (May 5, 2017), available at https://www.jointcommission.org/assets/1/6/Pain_Std_History_Web_Version_05122017.pdf.

²⁰ Federation of State Medical Boards of the U.S., Inc., *Model Policy for the Use of Controlled Substances for the Treatment of Pain* (May 2004), available at https://www.ihs.gov/painmanagement/includes/themes/newihstheme/display_objects/documents/modelpolicytreatmentpain.pdf.

²¹ See *Oregon Board Disciplines Doctor for Not Treating Patients’ Pain*, N.Y. Times (Sept. 14, 1999), <https://www.nytimes.com/1999/09/04/us/oregon-board-disciplines-doctor-for-not->

cases, and others like them, illustrate a changing culture and a recognition that patients, especially those at the end of life, are entitled to adequate pain treatment.²²

Around this time, many state legislatures passed “intractable pain statutes,” providing prescribers some assurances by reducing the risk of regulatory sanctions for treating pain with controlled substances.²³ In Ohio, for example, O.R.C. § 4731.05.2, passed in 1997, required the state medical board to “adopt rules . . . that establish standards and procedures to be followed by physicians in the diagnosis and treatment of intractable pain, including standards for managing intractable pain by prescribing, personally furnishing, or administering dangerous drugs in amounts or combinations that may not be appropriate when treating other medical conditions.” The law further noted that “[a] physician who treats intractable pain by managing it with dangerous drugs is not subject to disciplinary action by the board under section 4731.22 of the Revised Code solely because the physician treated the intractable pain with dangerous drugs.”

Double-blind placebo-controlled studies published in the 1990s indicated that opioid medications were effective analgesics in the treatment of chronic non-cancer pain, and subsequent meta-analyses²⁴ in the 2000s analyzed these and other trials. Kalso and Eisenberg demonstrated analgesic efficacy for opioids in the “intermediate term” (Kalso: 4 days – 8 weeks; Eisenberg: 8-70 days). Furlan showed efficacy of both weak and strong opioids over placebo in both pain and function in noncancer pain patients. However, Martell, who studied only back pain patients, found opioids efficacious for short term relief, but it was unclear whether they were efficacious beyond 16 weeks in this population.²⁵

treating-patients-pain.html; Charatan F. Doctor disciplined for “grossly undertreating” pain. *BMJ*. 1999 Sep 18;319(7212):728.; *Doctor liable for not giving enough pain medicine*, CNN (June 14, 2001), <http://www.cnn.com/2001/LAW/06/13/elderabuse.lawsuit/index.html>.

²² Hoffmann DE, Tarzian AJ. Achieving the right balance in oversight of physician opioid prescribing for pain: the role of state medical boards. *J Law Med Ethics*. 2003 Spring;31(1):21-40.

²³ *Id.*

²⁴ Kalso E, Edwards JE, Moore RA, McQuay HJ. Opioids in chronic non-cancer pain: Systematic review of efficacy and safety. *Pain*. 2004;112:372–80; Eisenberg E, McNicol ED, Carr DB. Efficacy and safety of opioid agonists in the treatment of neuropathic pain of nonmalignant origin: Systematic review and meta-analysis of randomized controlled trials. *JAMA*. 2005;293:3043–52; Eisenberg E, McNicol E, Carr DB. Opioids for neuropathic pain. *Cochrane Database Syst Rev*. 2006;3:CD006146; Furlan A, Sandoval J, Mailis-Gagnon A, Tunks E. Opioids for chronic noncancer pain: A meta-analysis of effectiveness and side effects. *CMAJ*. 2006;174:1589–94; Martell BA et al. Systematic review: opioid treatment for chronic back pain: prevalence, efficacy, and association with addiction. *Ann Intern Med*. 2007 Jan 16;146(2):116-27; McNicol ED, Midbari A, Eisenberg E. Opioids for neuropathic pain. *Cochrane Database Syst Rev*. 2013 Aug 29;(8):CD006146.

²⁵ Fishbain DA, Cole B, Lewis J, Rosomoff HL, Rosomoff RS. What percentage of chronic nonmalignant pain patients exposed to chronic opioid analgesic therapy develop abuse/addiction

Structured reviews reached similar conclusions. Devulder²⁶ found that the use of opioids for chronic non-cancer pain improved quality of life. Bloodworth²⁷ found an improvement in overall function, including sleep, functionality and activities of daily living among patients taking opioids. In contrast, however, Nicholas²⁸ found that functional outcomes were inconsistent across studies.

Although there was some data pointing in either direction, the overall clinical picture given to physicians for many years was that chronic opioid analgesic therapy (COAT) was effective for pain and function in many chronic pain patients. As a result, COAT became prescribed more frequently, not only by pain medicine specialists, but by general practitioners and other medical specialists as well.²⁹ According to the CDC, opioid prescriptions hit their peak in 2010, but even seven years later, 17% of Americans filled at least one opioid prescription.³⁰

Recent guidelines by agencies and medical societies continue to recognize a role for opioid treatment for both cancer and non-cancer pain. In 2016, for example, the CDC put forth guidelines for physicians treating chronic pain outside of active cancer, palliative, and end-of-life care.³¹ Although the guidelines stated that nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain, they noted that patients need not “fail” those treatments to be given opioid therapy. Rather, “expected benefits to specific to the clinical context should be weighed against risks before initiating therapy.”³² The agency reaffirmed in 2019 that active cancer treatment, palliative care, end-of-life care, and treatment of sickle cell disease were not covered by these guidelines, and that the guidelines themselves were not intended to “deny any patients who suffer with chronic pain from opioid therapy as an option for pain management.”³³ Similarly, 2017 guidelines from the American Society of Interventional

and/or aberrant drug-related behaviors? A structured evidence-based review. *Pain Med.* 2008 May-Jun;9(4):444-59.

²⁶ Devulder J, Richarz U, Nataraja SH. Impact of long-term use of opioids on quality of life in patients with chronic nonmalignant pain. *Curr Med Res Opin.* 2005;21:1555–68.

²⁷ Bloodworth D. Issues in opioid management. *Am J Phys Med Rehabil.* 2005;84:S42–55.

²⁸ Nicholas MK, Molloy AR, Brooker C. Using opioids with persisting noncancer pain: a biopsychosocial perspective. *Clin J Pain.* 2006 Feb;22(2):137-46.

²⁹ *Id.*

³⁰ *Prescription Opioid Data*, CDC, <https://www.cdc.gov/drugoverdose/data/prescribing.html> (last visited May 10, 2019).

³¹ Dowell D, Haegerich TM, Chou R. CDC guideline for prescribing opioids for chronic pain--United States, 2016. *JAMA.* 2016 Apr 19;315(15):1624-45.

³² *Id.*

³³ Centers for Disease Control and Prevention, Letter from Deborah Dowell to Robert W. Carlson (Feb. 28, 2019), *available at* <https://static1.squarespace.com/static/>

Pain Physicians recognized that “[d]espite the lack of significant evidence of efficacy of long-term opioid therapy in chronic non-cancer pain, it is generally accepted that some patients improve and many of them function well at low doses. Thus, it is essential to maintain access to these medications and also apply appropriate risk management strategies.”³⁴

The current guidelines from the FSMB addressing the treatment of chronic, non-cancer pain similarly support the use of opioid analgesics under appropriate circumstances (including “when non-opioid and non-pharmacological options have not been effective”) and when appropriate safeguards are in place.³⁵

On April 9, 2018, the Medical Letter, a publication written to help health care providers establish the best patient care, put forth guidelines on treating patients with both cancer and non-cancer pain that integrated in part the CDC and ASIPP guidelines.³⁶ The Medical Letter guidelines include provisions for the use of opioid medications for severe, acute pain. In addition, the guidelines recognize that opioid medications may be necessary for chronic non-cancer pain that is non-responsive to other treatments. For severe chronic cancer pain, opioid medications are the medications of choice. Finally, opioid medications may be used for neuropathic pain that is severe and has not responded to other agents. The Medical Letter contains the most current recommendations for physicians.³⁷

V. Risks Associated with Opioid Use

Like all prescription medications, opioids have both benefits and potential risks and side-effects. Despite these risks, the FDA continues to approve opioid medications as safe and effective. That means that the overall benefit to the public health outweighs the potential risks. Physicians or medical staff must always educate patients on new medications, and opioid medications are no different. During consultations, physicians and/or staff will lay out the pros and cons of opioid medication management. The patient would be informed about the risk and the benefits of these medications.

54d50ceee4b05797b34869cf/t/5cad1544104c7b3919659150/1554847045928/2019_CDC_letter_to_NCCN_ASCO_ASH.pdf.

³⁴ Manchikanti L et al. Responsible, safe, and effective prescription of opioids for chronic non-cancer pain: American Society of Interventional Pain Physicians (ASIPP) Guidelines. *Pain Physician*. 2017 Feb;20(2S):S3-S92.

³⁵ Federation of State Medical Boards, *Guidelines for the Chronic Use of Opioid Analgesics* (Apr. 2017), https://www.fsmb.org/siteassets/advocacy/policies/opioid_guidelines_as_adopted_april-2017_final.pdf.

³⁶ Opioids for pain. *Med Lett Drugs Ther*. 2018 Apr 9;60(1544):57-64. The Medical Letter has no funding from industry and is viewed as objective, unbiased, and evidence-based.

³⁷ *Id.*

Before starting any opioid medications, a physician should consider alternative medications. These other medications may include nonsteroidal-based medications, antidepressant medications, antiseizure medications, and steroid medications. The patient may also have tried interventional therapy without improvement or the patient may have contraindication to interventional therapy. Notably, each of these alternative treatments carries its own set of risks and benefits. The risks associated with non-steroidal anti-inflammatory agents (NSAIDs) include myocardial infarction (MI), stroke, and bleeding. NSAIDs have been reported to have equivalent fatal adverse event rates to prescription opioids.³⁸

Respiratory depression is a serious, and potentially fatal, potential side-effect of opioids. As such, physicians are in a position to minimize this risk by careful patient selection, considering both the patient's co-morbidities (e.g., sleep apnea) and concomitant medications (e.g., benzodiazepines) that would put the patient at elevated risk. Because the risk of respiratory depression is also related to the dose of medication administered, it is good practice to prescribe the lowest effective dose to ensure that the patient can tolerate the medication. The risk of respiratory depression is also time-limited, meaning the risk reduces greatly after the patient has taken the same amount of medication for some period of time. It is also important to educate patients and their loved ones on the signs of respiratory depression and treatment.

Common nuisance adverse effects of opioid medication include constipation and nausea, which can be managed with an oral laxative or with a change in the patient's diet. Usually, the nausea and constipation are related and time-limited. Other risks of opioid medications include somnolence. These medications can affect patient cognition, causing sedation. Usually, this side effect is also time-limited.

Other major risks include physical tolerance and dependence, and addiction. The brain adapts to taking an opioid regularly, resulting in physical dependence. It is characterized by withdrawal symptoms when the opioid is taken away or the dose reduced, or upon administration of an opioid antagonist. Physical dependence and withdrawal can also be seen with other substances, such as alcohol or benzodiazepines. Physical dependence while taking opioids is normal and expected response to continuous opioid therapy, and can develop within a few days of dosing with opioids, although it varies among patients.

Physical dependence is not the same as addiction. A patient on chronic opioid therapy who is physically dependent but who does not have adverse behavioral problems will not meet the criteria for addiction or opioid use disorder. Addiction is defined as a chronic dysfunction of brain reward, motivation, memory, and related circuitry, leading to characteristic biological,

³⁸ Solomon DH, Rassen JA, Glynn RJ, Lee J, Levin R, Schneeweiss S. The comparative safety of analgesics in older adults with arthritis. *Arch Intern Med.* 2010 Dec 13;170(22):1968-76.

psychological, social, and spiritual manifestations. Addiction has the following criteria: 1) compulsive drug use, 2) loss of control, 3) cravings, and 4) continued use despite harm.³⁹

Like in other areas of medicine, each patient is unique when it comes to their potential risk of prescription opioid misuse and addiction. A review by Portenoy⁴⁰ concluded that addiction occurred not only because of the inherent reinforcing properties of the opioid drugs, but also because of the individual's predisposing psychological, social, and physiological factors. Certain demographic, background, and psychological factors have been identified as associated with an increased risk of misuse by chronic pain patients. Prescribing physicians are in the best position to establish and monitor these known risks, and to minimize the risk in the first place by careful patient selection. In fact, studies have demonstrated that fewer chronic opioid patients will suffer abuse and addiction if they are preselected for no previous or current history of drug or alcohol abuse or addiction.⁴¹

³⁹ Choi CY. Chronic pain and opiate management. *Dis. Mon.* 2016 Sep;62(9):334-45; American Psychiatric Association, *What Is Addiction?* (Jan. 2017), <https://www.psychiatry.org/patients-families/addiction/what-is-addiction>.

⁴⁰ Portenoy RK. Opioid therapy for chronic nonmalignant pain: a review of the critical issues. *J Pain Symptom Manage.* 1996 Apr;11(4):203-17.

⁴¹ Fishbain DA, Cole B, Lewis J, Rosomoff HL, Rosomoff RS. What percentage of chronic nonmalignant pain patients exposed to chronic opioid analgesic therapy develop abuse/addiction and/or aberrant drug-related behaviors? A structured evidence-based review. *Pain Med.* 2008 May-Jun;9(4):444-59.

Psychiatric disorders, including negative affect conditions such as anxiety and depression, are also associated with misuse.⁴² Reporting a high level of pain⁴³, pain sensitivity⁴⁴, and pain catastrophizing⁴⁵ are all associated with misuse.

⁴² Martel MO et al. Catastrophic thinking and increased risk for prescription opioid misuse in patients with chronic pain. *Drug Alcohol Depend.* 2013 Sep 1;132(1-2):335-41 (citing Dersh J et al. Prescription opioid dependence is associated with poorer outcomes in disabling spinal disorders. *Spine (Phila Pa 1976)*. 2008 Sep 15;33(20):2219-27; Edlund MJ et al. Do users of regularly prescribed opioids have higher rates of substance use problems than nonusers? *Pain Med.* 2007 Nov-Dec;8(8):647-56; Morasco BJ et al. Risk for prescription opioid misuse among patients with a history of substance use disorder. *Drug Alcohol Depend.* 2013 Jan 1;127(1-3):193-9; Schieffer BM et al. Pain medication beliefs and medication misuse in chronic pain. *J Pain.* 2005 Sep;6(9):620-9; Wasan AD et al. Psychiatric history and psychologic adjustment as risk factors for aberrant drug-related behavior among patients with chronic pain. *Clin J Pain.* 2007 May;23(4):307-15; Wilsey BL et al. Psychological comorbidities predicting prescription opioid abuse among patients in chronic pain presenting to the emergency department. *Pain Med.* 2008 Nov;9(8):1107-17; Edlund MJ et al. Risk factors for clinically recognized opioid abuse and dependence among veterans using opioids for chronic non-cancer pain. *Pain.* 2007 Jun;129(3):355-62; Grattan A et al. Depression and prescription opioid misuse among chronic opioid therapy recipients with no history of substance abuse. *Ann Fam Med.* 2012 Jul-Aug;10(4):304-11.).

⁴³ Martel MO et al. Catastrophic thinking and increased risk for prescription opioid misuse in patients with chronic pain. *Drug Alcohol Depend.* 2013 Sep 1;132(1-2):335-41 (citing Adams LL et al. Development of a self-report screening instrument for assessing potential opioid medication misuse in chronic pain patients. *J Pain Symptom Manage.* 2004 May;27(5):440-59; Grattan A et al. Depression and prescription opioid misuse among chronic opioid therapy recipients with no history of substance abuse. *Ann Fam Med.* 2012 Jul-Aug;10(4):304-11; Jamison RN, Link CL, Marceau LD. Do pain patients at high risk for substance misuse experience more pain? A longitudinal outcomes study. *Pain Med.* 2009 Sep;10(6):1084-94; Morasco BJ, Turk DC, Donovan DM, Dobscha SK. Risk for prescription opioid misuse among patients with a history of substance use disorder. *Drug Alcohol Depend.* 2013 Jan 1;127(1-3):193-9.).

⁴⁴ Edwards RR, Wasan AD, Michna E, Greenbaum S, Ross E, Jamison RN. Elevated pain sensitivity in chronic pain patients at risk for opioid misuse. *J Pain.* 2011 Sep;12(9):953-63.

⁴⁵ *Id.*; Jamison RN, Link CL, Marceau LD. Do pain patients at high risk for substance misuse experience more pain? A longitudinal outcomes study. *Pain Med.* 2009 Sep;10(6):1084-94; Morasco BJ et al. Risk for prescription opioid misuse among patients with a history of substance use disorder. *Drug Alcohol Depend.* 2013 Jan 1;127(1-3):193-9; Sullivan MJ et al. Theoretical perspectives on the relation between catastrophizing and pain. *Clin J Pain.* 2001 Mar;17(1):52-64; Martel MO et al. Catastrophic thinking and increased risk for prescription opioid misuse in patients with chronic pain. *Drug Alcohol Depend.* 2013 Sep 1;132(1-2):335-41.

Young age and history of previous substance abuse have been identified as risk factors for opioid misuse.⁴⁶ A 2015 survey found⁴⁷ that an estimated 18.9 million people aged 12 or older (7.1% of the population) had misused prescription psychotherapeutic drugs in the past year. Psychotherapeutic drugs included pain relievers, tranquilizers, stimulants, and sedatives. Prescription pain relievers were the most commonly misused, with 12.5 million (4.7% of the population) of people aged 12 or older misusing.⁴⁸ Notably, the 18-25 year old age group were likelier than those 12-17 or older than 26 to misuse prescription pain relievers and other psychotherapeutic drugs.⁴⁹ Also notably, the vast majority of patients who misused prescription opioid medications previously abused some other illicit substance. Depending on the time frame, 70-74% of patients who misused prescription opioids have a history of prior substance abuse.⁵⁰ This statement concerning polysubstance abuse cannot be overlooked—there is clear evidence in the addiction community that individuals will often abuse more than one substance. That is, individuals can demonstrate a behavior pattern that indicates they may be inclined to substance abuse.

Polysubstance abuse is related to the “gateway theory” of drug use—the idea that exposure to one substance can change a patient’s biologic and behavioral factors, leading to future use of other drugs. Although it has been theorized that prior use of opioids may lead to heroin use, the data do not support this being the case. First, data from the Substance Abuse and Mental Health Services Administration (SAMHSA), which is cited by plaintiffs’ experts, does demonstrate that almost 80% of patients who abused heroin previously abused prescription

⁴⁶ Edlund MJ et al. Risk factors for clinically recognized opioid abuse and dependence among veterans using opioids for chronic non-cancer pain. *Pain*. 2007 Jun;129(3):355-62; Michna E et al. Predicting aberrant drug behavior in patients treated for chronic pain: importance of abuse history. *J Pain Symptom Manage*. 2004 Sep;28(3):250-8; Ives TJ et al. Predictors of opioid misuse in patients with chronic pain: a prospective cohort study. *BMC Health Serv Res*. 2006 Apr 4;6:46; Morasco BJ, Dobscha SK. Prescription medication misuse and substance use disorder in VA primary care patients with chronic pain. *Gen Hosp Psychiatry*. 2008 Mar-Apr;30(2):93-9; Schieffer BM et al. Pain medication beliefs and medication misuse in chronic pain. *J Pain*. 2005 Sep;6(9):620-9.

⁴⁷ Hughes A et al. Prescription Drug Use and Misuse in the United States: Results from the 2015 National Survey on Drug Use and Health. *NSDUH DATA Review*. September 2016. Available at <https://www.samhsa.gov/data/sites/default/files/NSDUH-FFR2-2015/NSDUH-FFR2-2015.htm>.

⁴⁸ *Id.*

⁴⁹ *Id.*

⁵⁰ Muhuri PK, Gfroerer JC, Davis CM. Associations of Nonmedical Pain Reliever Use and Initiation of Heroin Use in the United States, at 15 tbl. 6. *CBHSQ Data Review*. August 2013. Available at <https://www.samhsa.gov/data/sites/default/files/DR006/DR006/nonmedical-pain-reliever-use-2013.pdf>.

opioid medications.⁵¹ The same study, however, shows that only 3.6% of patients who abuse prescription opioid medications go on to initiate heroin use with the next 5 years.⁵² We also know from other SAMHSA data that patients who abuse prescription opioids represent only a small fraction of those who receive legitimate prescriptions for these medications.⁵³ The SAMHSA data also show that most patients who abused prescription opioids previously abused some other illicit substance. Therefore, the vast majority of most patients for whom prescription opioids are prescribed do not become abusers of legal or illegal opioids.⁵⁴ And the assertion that prescription opioid use commonly or frequently results leads to heroin use is unsupported in the medical literature.

A prescribing clinician should employ a validated screening tool to assess for risk of aberrant drug-related behaviors, such as the Screener and Opioid Assessment for Patients with Pain Revised (SOAPP-R) or the Opioid Risk Tool (ORT) H-15. If patients are at increased risk, that does not necessarily preclude them from being candidates for opioid therapy. Identifying the increased risk at the outset, however, enables the prescriber to more closely monitor the patient during the course of treatment.⁵⁵ In addition to re-enforcing the opiate agreement, other reasonable options for managing those patients identified at higher risk for misuse include setting limits, increasing the frequency of visits, providing only a very limited supply of a medication, prescribing long-acting opiates with lower street value, more frequently performing urine drug screens, counting pills, and referring to a psychologist.⁵⁶

VI. Dosage and Overdose

Opioid medication abuse has become a significant public health problem in the United States, and since 1999 we have seen a nearly six-fold increase in deaths from unintended opioid overdoses.⁵⁷ Recent data, however, shows that the number of opioid prescriptions actually decreased by 19% from 2006 to 2017, even while the overall opioid overdose rate continues to

⁵¹ *Id.* at 11 tbl.3.

⁵² *Id.* at 14.

⁵³ Hughes A et al. Prescription Drug Use and Misuse in the United States: Results from the 2015 National Survey on Drug Use and Health. *NSDUH DATA Review*. September 2016. Available at <https://www.samhsa.gov/data/sites/default/files/NSDUH-FFR2-2015/NSDUH-FFR2-2015.htm> (“12.8% of people aged 12 or older who used pain relievers in the last year reported misuse.”).

⁵⁴ *Id.*

⁵⁵ Nicholson B, Passik SD. Management of chronic noncancer pain in the primary care setting. *South Med J.* 2007 Oct;100(10):1028-36.

⁵⁶ Choi CY. Chronic pain and opiate management. *Dis. Mon.* 2016 Sep;62(9):334-45.

⁵⁷ *Overview of the Drug Overdose Epidemic: Behind the Numbers*, CDC, <https://www.cdc.gov/drugoverdose/data/index.html> (last visited May 10, 2019).

rise.⁵⁸ This statistic is exceptionally important. While physicians and other practitioners have decreased the number of prescriptions being written, we still see an increasing number of deaths from overdoses—mainly due to heroin and illegal synthetic drugs such as homemade fentanyl.⁵⁹

A recent article from the American Journal of Public Health might shed some light on this curious finding.⁶⁰ The article's author, Dr. Seth, takes the position that the majority of recent overdose deaths are likely due to synthetic opiates, such as fentanyl-like drugs, mixed with other street drugs. Some toxicology reports, particularly prior to the rise in illicit fentanyl, cannot distinguish between medical fentanyl or illicitly mixed fentanyl. Of note, death certificates often contain limited information about the specific drug or drugs involved in an overdose death and do not distinguish between drugs pharmaceutically manufactured and legitimately prescribed, drugs pharmaceutically manufactured but not legitimately prescribed, and drugs illicitly manufactured. This means that the statistics obtained from death certificate data likely are not as robust as they appear in putting blame on opioid medications. In 2014, multiple drugs were involved in almost half of the drug overdose deaths where the death certificate mentioned at least one specific drug. Therefore, it is nearly impossible to attribute the cause of death to opioid medications alone, since other drugs may have been involved. Dr. Seth states that, to determine how to treat a drug crisis, it is imperative that we first understand the drugs being used and the specific effects those drugs are causing. Only when we determine the combination of drugs that leads to an untimely death can we address the crisis appropriately.⁶¹

Because the development of tolerance varies among individuals, there is no absolute limit to opioid medication dose. Higher-dose opioid therapy (i.e. daily doses of 100mg or more morphine equivalents) is so defined based on elevated risks associated with certain doses.⁶²

Fortunately, a variety of organizations have addressed dosage levels by developing pain guidelines. These organizations and guidelines include the Clinical Guidelines for the Use of Chronic Opioid Therapy in Chronic Noncancer Pain, the International Association for the Study of Pain Guidelines, the World Health Organization's Treatment Guidelines on Pain, and the American Academy of Pain Medicine.⁶³ While available guidelines vary, many provide

⁵⁸ *Prescription Opioid Data*, CDC, <https://www.cdc.gov/drugoverdose/data/prescribing.html> (last visited May 10, 2019); *Overdose Death Rates*, National Institute on Drug Abuse, at fig. 3 (Jan. 2019), <https://www.drugabuse.gov/related-topics/trends-statistics/overdose-death-rates>.

⁵⁹ Seth P, Rudd RA, Noonan RK, Haegerich TM. Quantifying the epidemic of prescription opioid overdose deaths. *Am J Public Health*. 2018 Apr;108(4):500-502.

⁶⁰ *Id.*

⁶¹ *Id.*

⁶² Kobus AM, Smith DH, Morasco BJ, Johnson ES, Yang X, Petrik AF, Deyo RA. Correlates of higher-dose opioid medication use for low back pain in primary care. *J Pain*. 2012 Nov;13(11):1131-8.

⁶³ Chou R et al.; American Pain Society-American Academy of Pain Medicine Opioids Guidelines Panel. Clinical guidelines for the use of chronic opioid therapy in chronic noncancer

validated methodologies for using opioid medications to address chronic pain, including recommendations for physicians to determine a patient's risk, initiate and monitor prescriptions, escalate dosage, and other recommendations that can be used to safeguard a patient from abuse and addiction.

Higher doses of opioids subject patients to greater risk, and perhaps without added benefit.⁶⁴ Patients on high-dose opioid therapy may be at greater risk of side effects, addiction, misuse, and possibly diversion. They may also experience unique side effects, such as endocrinologic abnormalities, arrhythmia (with methadone), and fracture risk.

Notably, higher doses are associated with increased risk of overdose and death. Kobus found that high-dose opioid therapy is associated with other risk factors, such as multiple pain diagnoses and other medical, mental health, and substance use comorbidity.⁶⁵

This data demonstrates that opioid medications themselves are not inherently dangerous; rather, it is the dose, patient selection, and other medications provided to the patient that may cause lethality.

Unfortunately, studies have shown that patients with comorbid psychiatric diagnoses tend to receive higher-dose opioid prescriptions. These patients are likelier to receive both long-term opioid therapy and higher doses. However, this patient population is often excluded from clinical trials and so evidence-based guidance is lacking on how to prescribe opioids to this population.⁶⁶

Regardless of the paths abusers and addicts take, there is a clear need for medical providers to carefully screen opioid therapy candidates for mental health disorders and SUDs and either treat or refer them for specialty mental health care. The hope is to avoid pairing higher-dose therapy with high-risk patients.⁶⁷

pain. *J Pain*. 2009 Feb;10(2):113-30; *IASP Guidelines*, International Association for the Study of Pain, <https://www.iasp-pain.org/Guidelines?navItemNumber=648> (last visited May 10, 2019); *Treatment Guidelines on Pain*, World Health Organization, https://www.who.int/medicines/areas/quality_safety/guide_on_pain/en/ (last visited May 10, 2019); *AAPM Pain Treatment Guidelines*, American Academy of Pain Medicine, <https://painmed.org/clinician-resources/clinical-guidelines> (last visited May 10, 2019).

⁶⁴ Kobus AM, Smith DH, Morasco BJ, Johnson ES, Yang X, Petrik AF, Deyo RA. Correlates of higher-dose opioid medication use for low back pain in primary care. *J Pain*. 2012 Nov;13(11):1131-8.

⁶⁵ *Id.*

⁶⁶ *Id.*

⁶⁷ *Id.*

VII. National Response to Opioid Epidemic

Over the past 30 years, the illegal drug trade has matured into a massive, global distribution network whose breadth and efficiency has never before been seen. Illegal drug manufacturers have generally moved away from agriculturally-produced products such as cannabis, cocaine, and heroin, and toward synthetic drugs such as methamphetamines and fentanyl. These new synthetics are generally cheaper, easier to produce, more potent, and more accessible to a wider range of users.⁶⁸

At the same time, the number of legitimate opioid medication prescriptions has grown considerably. Alongside the growth of legitimate prescriptions, prescribers' concerns related to adverse effects, misuse and abuse, morbidity and mortality, and scrutiny by federal and state regulatory agencies have been escalating. Cognizant of the growing concerns about morbidity and mortality associated with opioid abuse and misuse, the United States Congress has mandated that the FDA develop a comprehensive strategy for monitoring opioid use, morbidity, and mortality. In response, FDA has developed Risk Evaluation and Mitigation Strategies (REMS), including the provision of training for physicians on appropriate prescribing and use of certain opioids, as well as guidelines for companies that market centrally-acting drugs like opioids. Moreover, several pharmaceutical companies have developed tamper-resistant formulations (TRFs), though the actual influence and effectiveness of TRFs on provider beliefs and practices is unknown.⁶⁹

Since 2007, the FDA has requested that manufacturers of opioid medications develop risk evaluation and mitigation strategies (REMS) for products under review. In 2011 the FDA and the Office of National Drug Control Policy mandated the development of REMS within 120 days to address those concerns. Part of the manufacturers' obligations is to financially support CME programs to prescribers of opioids, educating them on risks and benefits, appropriate patient selection, counseling on safe use, recognizing misuse, abuse, and addiction.⁷⁰ On July 9, 2012, the FDA approved the final REMS, including a Prescriber Education program, for extended release/long-acting opioids.⁷¹

⁶⁸ DuPont RL. The opioid epidemic is an historic opportunity to improve both prevention and treatment. *Brain Res Bull.* 2018 Apr;138:112-114.

⁶⁹ Wilson HD, Dansie EJ, Kim MS, Moskovitz BL, Chow W, Turk DC. Clinicians' attitudes and beliefs about opioids survey (CAOS): instrument development and results of a national physician survey. *J Pain.* 2013 Jun;14(6):613-27.

⁷⁰ *Pain Management and Opioid Abuse: A Public Health Concern*, American Academy of Family Physicians, available at https://www.aafp.org/dam/AAFP/documents/patient_care/pain_management/opioid-abuse-position-paper.pdf.

⁷¹ U.S. Food & Drug Admin., Questions and Answers: FDA approves a Risk Evaluation and Mitigation Strategy (REMS) for Extended-Release and Long-Acting (ER/LA) Opioid Analgesics

Another attempt to limit the number of opioid medications provided to patients was in the rescheduling of hydrocodone-like medications. In 1973, following the establishment of the Drug Enforcement Administration (DEA), heroin was categorized into Schedule I as a substance with no currently accepted medical use and high potential for abuse. Most opioids used for pain management fall into Schedule II as a substance with high potential for abuse. In late 2014, the DEA “up-scheduled” hydrocodone from Schedule III, with moderate-to-low potential for physical or psychological dependence, to Schedule II in direct response to concerns about abuse of this medication.⁷²

Failing to recognize that the drug abuse problem in our country—including the overdose death problem—involves far more than prescription opioids can lead to a misguided response to the problem. Massive bipartisan support to turn back the nation’s drug epidemic can lead to the development of new and better ways to prevent and to treat addiction. Physicians and other practitioners writing opioid prescriptions may not currently be sufficiently educated on the tools that can be used to assess ongoing addiction or the potential for addiction.

Alongside improvements in understanding of opioid medications and the implementation of refined patient assessment, physicians must understand that chronic pain management ideally involves a team-based approach and does not rely solely on prescription-based management.

VIII. Conclusion

Based upon my review of the extensive medical literature on the topic and my many years of experience serving as a board certified anesthesiologist, pain medicine specialist, and addiction specialist, I offer opinions that include the following:

Opioid medication is neither “all good” nor “all bad.” Like all medications, prescription opioids have both risks and benefits. We have a better understanding at present of the overall risks and benefits of these classic medications than we have had in the past.

Opioid medications are effective for the treatment of chronic nonresponsive pain in many patients, especially after conservative therapy with other types of medications have failed. This understanding is reflected in, for example, leading guidelines, policies, and consensus statements.

Physicians must evaluate the risks and benefits of prescription opioids for each individual patient based upon that patient’s unique background, needs, and risk factors. As with most

(Mar. 1, 2013), <https://www.fda.gov/drugs/information-drug-class/questions-and-answers-fda-approves-risk-evaluation-and-mitigation-strategy-rems-extended-release-and>.

⁷² Schedules of Controlled Substance: Rescheduling of Hydrocodone Combination Products from Schedule III to Schedule II, 79 Fed. Reg. 49,661 (Aug. 22, 2014), *available at* https://www.deadiversion.usdoj.gov/fed_regs/rules/2014/fr0822.htm; Crawford, Chris, *How Will Rescheduling of Hydrocodone Combo Products Affect You, Your Patients?*, American Academy of Family Physicians (Sept. 17, 2014), <https://www.aafp.org/news/health-of-the-public/20140917hcps-sked2.html>.

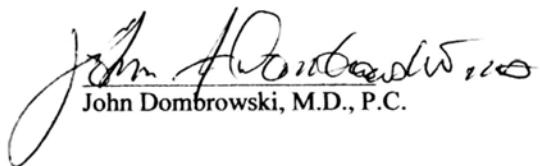
medications, physicians must implement a variety of risk mitigation strategies to effectively capture the benefits of opioid medications while minimizing risks to the patient.

As a result of developing medical standards and research, physicians now have better tools to both identify patients who are at potential risk for dependency as well as tools to assist individuals who become psychologically dependent. These tools can be used in a two-pronged approach—recognizing potential risk and establishing appropriate treatment when necessary—to improve patient outcomes related to prescription opioid treatment.

I reserve the right to amend my report and review additional materials as they become available.

10 May 2019

Date



John Dombrowski, M.D., P.C.

EXHIBIT A

CURRICULUM VITAE

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EDUCATION

8/1985 – 5/1989	Doctor of Medicine Georgetown University School of Medicine Washington, DC
8/1983 - 5/1985	Master of Science, Physiology Georgetown University Washington, DC
8/1980 - 5/1984	Bachelor of Science, Biology Minor in Chemistry, Cum Laude University of Richmond Richmond, VA

POST GRADUATE EDUCATION

7/1990 – 6/1993	Anesthesiology Yale – New Haven Hospital New Haven, CT
7/1989 – 6/1990	Internal Medicine Yale University St. Mary's Hospital, Waterbury Hospital Waterbury, CT
7/2000 – 1/2001	Medical Acupuncture University of California Los Angeles, CA

SPECIALTY TRAINING

Pain Medicine
Cardiothoracic Anesthesia
Obstetrical Anesthesia
Medical Acupuncture
Addiction Medicine

EMPLOYMENT

10/2004 – Present	John F. Dombrowski, MD, PC The Washington Pain Center
8/2012 - Present	Program Development, Anesthesiologist Assistant, Case Western Reserve Adjunct Assistant Professor, Case Western Reserve
12/2015- Present	Medical Director Outlook, Bayside Methadone Recovery & Tranquility Woods
7/2010 – 11/2018	Providence Hospital, Staff Anesthesiologist Washington, DC
8/1995 – 12/2004	Certified Anesthesia Services, LLC, <i>Partner</i> Sibley Memorial Hospital Director, Center for Pain Medicine Pain Medicine, cancer and chronic pain
8/1995 – 3/1996	Office Based Anesthesia Services, PC, <i>Founder</i> First office based practice of anesthesiology in Richmond, VA Pediatric, adult restorative dentistry and office surgeries
7/1993 – 7/1995	Piedmont Anesthesia Specialists, PC Director and Founder of the Chronic Pain Services for Chippenham Medical Center Developer of the acute epidural catheter pain service for Chippenham and Richmond Memorial Hospitals

LICENSE & CERTIFICATION

Fellow of the American Society of Anesthesiologists

Diplomate American Board of Anesthesiology (*recertified*)

Diplomate American Board of Pain Medicine (*recertified*)

Diplomate American Board of Addiction Medicine

Diplomate American Board of Preventive Medicine

Diplomate National Board of Medical Examiners

Advanced, Pediatric and Basic Life Support Certificate

Medical License: District of Columbia, Maryland, Virginia& Florida

Acupuncture License: District of Columbia

Strathmore Who's Who worldwide Lifetime member

PROFESSIONAL MEMBERSHIPS

American Society of Anesthesiology:
Secretary, 2014-2018
Director, Board of Directors, 2003-2014
Section on Fiscal Affairs, 2013-present
Ad Hoc Committee on Health Policy Research Institute, 2010-2012
Ad Hoc Committee on Web Oversight, 2012-present
Ad Hoc Committee on Public Outreach, 2003-2005, 2006-2008
Ad Hoc Committee on the Future of Pain Medicine, 2008-2010
House of Delegates Reference Committee on Administrative Affairs 2009-2013
House of Delegates Reference Committee Financial Affairs 2013-present
Committee on Administrative Affairs, 2007-2011.
Committee on Anesthesia Care Team, 1998-1999, 2000-2003, 2005-2009
Committee on AA Education and Practice, 2006-2010
Committee on Communications, 2003-2009; Chair 2009-2013
Committee on Economics, 2008-2010.
Committee on Finance, 2013-present.
Committee on Governmental Affairs, 2012-present
Committee on Membership, 2013-present
Committee on Newsletter, 2009-2013
Committee on Outreach Education, 2008-2009
Committee on Pain Medicine, 2006-present
Committee on Professional Education Oversight, 2010- 2012
Mid Atlantic Caucus, Secretary-Treasurer, 2011-present
ASAPAC Independent Expenditure Unit, 2008-2012
ASAPAC Board 2008-2011
Task Force on State Advocacy, 2013
ASA Public Relations DVD Outreach on Awareness, 2008
Subcommittee Chairman: Regional Anesthesia and Non-Physician Providers
ASA Policy Statement 2008
Recipient AAAA Distinguished Service by a Physician Award, 2011
Subcommittee on Communication, Public Outreach and Professionalism, 2009
Chairman: Accreditation Review Committee for the Anesthesiologist Assistant

District of Columbia Society of Anesthesiologists
President, 2004-2006
President-elect, 2002-2003
Secretary-Treasurer, 1996-2002
Active Member, 1997-present

Richmond Society of Anesthesiologists
Secretary Treasurer, 1994 – 1996
Public Relations and Legislative Committees, 1993-1996

PROFESSIONAL MEMBERSHIPS

Editorial Board, Outpatient Surgical Magazine
President and *Founder*, Washington Pain Society
Washington Society of Electroconvulsive Therapy
National Eagle Scout Association
Washingtonian Magazine *Top Doctor*, 2002- present
Patient Choice Awards Physician, 2007- present

Academic and Media Presentations

July 2018	Federal Occupational Health, “Understanding Pain Management and Addiction”
June 2018	DC Bar Association, “Legal Ethics, Substance Use and the Opioid Crisis” Washington, DC
December 2017	DC Bar Continuing Legal Education, “Opioid addiction and the professional” Washington, DC
October 2017	University of Maryland Health Center, “Treating addiction in young adults” College Park, Maryland
August 2017	West Virginia Society of Anesthesiologists Annual Meeting “Pain Medicine and Addiction for the Anesthesiologist: Understanding the need to treat and change anesthesia management” White Sulphur Springs, WV
July 2017	Voice of America Media presentation on treatment of chronic pain without opiates. Washington, DC
July 2017	Fox Business News “The opiate crisis in America and the Trump Administration” Washington, DC
June 2017	Florida Society of Anesthesiologists Annual Meeting “Pain Medicine and Addiction for the Anesthesiologist: Understanding the need to treat and change anesthesia management” and Update in the ASA Palm Beach, FL

April 2017	National Drug Abuse and Heroin Summit “Pain Management Outside of Narcotic Therapy” Atlanta, GA
April 2016	Iowa Society of Anesthesiologists Spring Meeting “Pain Medicine and Addiction for the Anesthesiologist: Understanding the need to treat and change anesthesia management” and Update in the ASA Des Moines, IA
August 2016	West Virginia Society of Anesthesiologists, “ASA Update 2016” White Sulphur Springs, WV
October 2015	District of Columbia Society of Anesthesiologists “Pain Medicine and Addiction for the Anesthesiologist: Understanding the need to treat and change anesthesia management” and Update in the ASA Washington, DC
September 2015	Visiting Professor Grand Rounds SUNY Buffalo “ASA update 2015 membership” Buffalo, NY
July 2015	American Education Institute Inc. “Diagnosing and Managing Chronic Pain for Primary Care Physicians”
November 2014	Presentation before the FDA on the safety of epidural steroid usage. Silver Spring, MD
November 2014	Metropolitan Washington Assn of Occupational Health Nurses “Pain Management New Paradigms, New Treatments, Better Results” Washington, DC
August 2014	Is CAM a Sham? Understanding Complementary and Alternative Medicine for the Practicing Anesthesiologists, ASA Newsletter
June 2013	International Neuromodulation Society Neuromodulation 11 th World Congress “Spinal cord stimulation offers a safe and effective therapeutic option for chronic diabetic neuropathic pain and post chemotherapeutic induced pain” Berlin, Germany
December 2012	New York Society of Anesthesiologists Post Graduate Assembly (PGA) “Update on the fungal contamination in steroid medication use in pain management” New York, NY
December 2012	Maryland Medical Society Med Chi “Medical-Legal Considerations in Treating Pain: Current and Future Trends” Baltimore, MD

October 2012	Annual ASA meeting Panelist, "The media response to the death of Michael Jackson" Moderator, "Update on the fungal contamination in steroid medication use in pain management" Washington, DC
July 2012	American Podiatric Medical Association National Meeting "Using preemptive analgesia for better patient outcomes" Washington, DC
May 2012	International Conference on Interventional Pain Medicine & Neuromodulation Abstract Presentation: "Neuromodulation and the treatment of Diabetic and Chemo induced Neuropathy, Seven patients with 80% improvement." Gdansk, Poland
January 2012	Texas Podiatry Medical Association "Treatment of Chronic Neuropathic Foot Pain: Medications and Stimulation" Plano, TX
February 2011	Drexel University College of Medicine / Hahnemann University Hospital Department of Anesthesiology "Treatment of Post Laminectomy Pain Syndrome and other therapies for neuropathic pain" Philadelphia, PA
October 2010	Georgetown University Departments of Neurosurgery/Neurology Grand Rounds "Options for patients with Post laminectomy Syndrome, the role of spinal stimulation" Washington, DC
July 2010	American Podiatric Medical Association -National Meeting "New treatments for diabetic/peripheral neuropathy" Seattle, WA
March 2010	Chronic Lower Extremity Pain: New Options for Treatment Chicago, IL
January 2010	American Association of Podiatry Medicine New York Meeting "Using Spinal Stimulation for diabetic neuropathy" New York, NY
November 2009	WUSA Channel 9, 'Treating patient's pain without opioids'
September 2009	Good Morning America, "The Death of Michael Jackson: Should patients be concerned about the safety of propofol?"
September 2009	Outpatient Surgery magazine, Excellence in the Operating room Pain management in the ASC setting San Francisco, CA

September 2009 American peripheral nerve surgeons meeting
“Introduction of Spinal Stimulation into your practice”
Ft Worth, TX

July 2009 American Podiatry Medical Association national meeting
“Spinal stimulation in patient with chronic foot pain”
Toronto, Canada

January 2009 ASA Newsletter article “Changes in and with the ASA,
The release of the New ASA branding campaign”

December 2008 ABC News Now, “Can your body predict the weather?”

November 2008 ABC News Now, “Aggressive Pain Management therapies’

October 2008 Utah Society of Anesthesiologists, Annual Meeting Key Note Address
“Bring Anesthesiologists Assistants to your state,
The challenges and rewards”
Salt Lake City, UT

August 2008 WJLA Channel 7 medical news “First implantation of
‘Eon mini’ in Washington Metropolitan area for back pain”

April 2008 Georgetown University Neurology/Neurosurgery Departments
Grand Rounds *Neuromodulation and patient selection*
Washington, DC

March 2008 *Neuromodulation and the Podiatric patient* an introduction to
Washington Podiatric Society monthly meeting.

February 2008 ASA monthly Newsletter *Communicating in the Public Eye*
How to speak with patients about concerns on awareness.

January 2008 *Clemens' implausible deniability*, Roger Clemens pain
Management techniques and Steroids interview ESPN web site.

December 2007 Star Jones Court TV Interview on the movie “*Awake*”
New York, New York

October 2007 Lecture on effective pain management in patients on workers’ compensation.
Traveler Insurance
Chantilly, Virginia

October 2007 Outpatient Surgery Magazine article
Kick your pain Services up a Notch

August 2007 USA Today Newspaper
Outpatient Surgical centers and safety

June 2007 Advanced Neuromodulation System
Moderator, Advanced topics symposia
Alexandria, Virginia

May 2007 Interventional Pain Institute workshop
Moderator
Bethesda, Maryland

April 2007 Introduction into Spinal Cord Stimulation for Neurologists
The Neurology Center
Washington, DC

April 2007 Outpatient Surgery Magazine article
Why should you Add Pain Medicine to your ASC Program

April 2007 Guest Lecturer American Academy of Anesthesiologist
Assistants 31st Annual Conference Airway Management and
Neuroaxial Blockade
Daytona Beach, Florida

April 2007 Foundation for Ambulatory Surgery in America
Annual meeting speaker
*The Role of the Anesthesiologist in OR Management and
Conflict Resolution*
New Orleans, Louisiana

January 2007 ASA DVD – Host for public outreach on awareness
10 minute video

January 2007 Grand Round – Suburban Hospital
Bethesda, MD
*General Understanding of Neuro-Modulation for the Primary
Medical Doctor*

December 2006 Outpatient Surgery Magazine article
What's New for Anesthesia and Pain Management?

November 2006 Lecture to Physical Therapists – Shady Grove Adventist Hospital
Rockville, MD
Neuro-modulation and Patient Selection for this Procedure

October 2006 National Hospice forum on Pain Management
Interventional techniques on management of cancer pain
Fairfax, Virginia

August 2006 Outpatient Surgery Magazine article
Review your Regional Protocol, Manger's guide to Regional anesthesia

June 2006	Careers in Anesthesiology, the Future of the Specialty National Youth Leadership Forum – Georgetown University Washington, DC
June 2006	Riderwood Retirement Facility Silver Spring, MD <i>New Techniques in Treating Chronic Pain with an Emphasis on Spinal Cord Stimulation</i>
May 2006	Voted by Checkbook Magazine Top Doctor in Pain Medicine and Anesthesiology sixth year in a row
April 2006	Outpatient Surgery Magazine article <i>Thinking of buying ambulatory Pain pumps</i>
March 2006	Grand Round – Mid-Atlantic Palliative Care <i>Interventional Pain Management and End of Life</i> Arlington, Virginia
February 2006	Today Show – Discussing death of Coretta Scott King, seeking Medical attention outside the United States
December 2005	Outpatient Surgery Magazine article <i>What's New for Anesthesia and Pain Management?</i>
August 2005	Keynote address – Massachusetts Avenue Surgical Center Bethesda, MD <i>21st Century Pain Management Techniques for the Outpatient Setting</i>
July 2005	Today Show – Discussing the safety of NSAIDs and patients with chronic pain
July 2005	Outpatient Surgery Magazine article <i>Pump up your pain management Guide to surgical drugs</i>
May 2005	WUSA, CBS Washington affiliate segment <i>Rechargeable Spinal Cord Stimulation and Patient Options</i>
April 2005	Today Show – Pain Management week series March 21 and April 1 Discussion on integrative pain medicine and round table email Discussion
April 2005	Today Show – Interview on Bextra and the FDA warning for patients
April 2005	WRC Channel 4 – Interview on the FDA warnings and alternative treatments for chronic pain
February 2005	Public Outreach ‘Oasis’ Suburban Program <i>New Techniques in Pain Management</i>

February 2005	WTTG Channel 5 – Interview <i>Awareness under Anesthesia: What can be done?</i>
December 2004	Outpatient Surgery Magazine lead article <i>New Devices in Anesthesiology</i>
October 2004	WTTG Channel 5 Interview on spinal cord stimulation and New technologies for chronic pain control
October 2004	WRC Channel 4 – Interview <i>Awareness under Anesthesia</i> ASA policy statement
September 2004	Osler Society – Discussion of the use of COX 2 and preoperative pain control Washington, DC
August 2004	The Washington Times lead article in Metro section <i>Conscious Sedation and the role of the Anesthesiologist</i>
May 2004	Greater Washington DC Support Group for Dystonia Washington, DC Pain Medicine and Management lecture
April 2004	American Association of Anesthesiologist Assistants annual meeting – Speaker, San Diego, CA
March 2004	Testimony before the DEA concerning prescribing opioids to patients over the internet, the ASA's position
November 2003	Cox Cable – Live interview <i>Awareness under Anesthesia</i>
October 2003	WJLA Television – Interview <i>Awareness under Anesthesia</i>
October 2003	Orthopedic Today – Interview Use of the BIS Monitor
June 2003	National Youth Leadership Forum - Lecture Georgetown University, Washington, DC <i>The Role of the Anesthesiologists</i>
November 2002	Voted by Washingtonian Magazine Top Doctor in Pain Medicine
April 2002	John P Kennedy Institute - <i>Pain Management in Patients with Developmental Disabilities</i> Georgetown University, Washington, DC

March 2001 Resident Grand Round – SUNY
 Buffalo, NY
 Inhalation Anesthesia in the 21st Century

February 2001 Washington Hospital Center – Cancer Institute
 Washington, DC
 Management of Complex Cancer Pain

July 2000 The Learning Channel – Science Live
 One hour live television
 Breakthrough in Pain Management for the 21st Century

June 1999 Sibley Memorial Hospital – Community education lecture
 Washington, DC
 Oh, my Aching Back: The Diagnosis and Treatment of Back Pain

January 1998 Commentator for Abbott Labs
 Washington, DC
 The Practical use of Sevoflurane in the Community Setting

December 1997 Sibley Memorial Community Outreach – Lead article
 Circulation 300,000
 Washington, DC
 On Health

November 1997 Sibley Memorial Hospital – Outreach lecture
 Washington, DC
 Cancer and Chronic Pain Management

September 1997 Liaison instruction for 4th year German medical student
 Sibley Memorial Hospital
 Washington, DC

July 1995 Richmond Society of Post Anesthesia Care
 Nursing regional meeting
 Richmond, VA
 Pharmacology and Physiology of Acute Pain Management in the PACU

March 1994 Cardiology Grand Round – Chippenham Medical Center
 Richmond, VA
 Techniques for Sedation and Analgesia in the Cardiac Catheterization Lab

November 1993 HCA Columbia infomercial
 Acute Pain Management and Epidural Pain Management
 Healthbreak

September 1993 WRVA – Radio talk show
 Richmond Academy of Radio
 Richmond, VA
 Ask the Doctor: Anesthesia and Pain Management

July 1993

Chippenham Medical Center – Lecture to all nursing staff
Richmond, VA
Epidural Catheter Usage in Acute Pain Management

EXHIBIT B

TESTIMONY LIST (LAST FOUR YEARS)

John Dombrowski, MD

Testimony List (last four years)

Depositions

May 2018 — Washington University vs. Dr. Anthony Guraino (St. Louis, MO)

February 2018 - Brazzell vs. Emory (Atlanta, GA)

August 2017 — Blue Cross Blue Shield vs, Millennium Laboratories (Los Angeles, CA)

April 2016 — Schoonmaker vs. Minassian (Hunt Valley, Maryland)

EXHIBIT C
MATERIALS CONSIDERED

AAPM Pain Treatment Guidelines, American Academy of Pain Medicine, <https://painmed.org/clinician-resources/clinical-guidelines> (last visited May 10, 2019).

American Academy of Family Physicians et al., *Promoting Pain Relief and Preventing Abuse of Pain Medications: a Critical Balancing Act* (2001), available at <https://www.deadiversion.usdoj.gov/pubs/advisories/painrelief.pdf>.

American Psychiatric Association, *What Is Addiction?* (Jan. 2017), <https://www.psychiatry.org/patients-families/addiction/what-is-addiction>.

Baker DW, *The Joint Commission's Pain Standards: Origins and Evolution* (May 5, 2017), available at https://www.jointcommission.org/assets/1/6/Pain_Std_History_Web_Version_05122017.pdf.

Centers for Disease Control and Prevention, letter from Deborah Dowell to Robert W. Carlson (Feb. 28, 2019), available at https://static1.squarespace.com/static/54d50ceee4b05797b34869cf/t/5cad1544104c7b3919659150/1554847045928/2019_CDC_letter_to_NCCN_ASCO_ASH.pdf.

Crawford, Chris, *How Will Rescheduling of Hydrocodone Combo Products Affect You, Your Patients?*, American Academy of Family Physicians (Sept. 17, 2014), <https://www.aafp.org/news/health-of-the-public/20140917hcps-sked2.html>.

Doctor liable for not giving enough pain medicine, CNN (June 14, 2001), <http://www.cnn.com/2001/LAW/06/13/elderabuse.lawsuit/index.html>.

Declaration of Russell K. Portenoy, MD, *In Re National Prescription Opiate Litigation*, MDL No. 2804, Dec. 13, 2018.

Expert Report, Anna Lembke, MD, *In Re National Prescription Opiate Litigation*, MDL No. 2804, Mar. 25, 2019.

Expert Report of Jane C. Ballantyne, MD, FRCA, *In Re National Prescription Opiate Litigation*, MDL No. 2804, Mar. 25, 2019.

Expert Report of Mark A. Schumacher, MD, Ph.D., *In Re National Prescription Opiate Litigation*, MDL No. 2804, Mar. 25, 2019.

Expert Report of Theodore Parran, *In Re National Prescription Opiate Litigation*, MDL No. 2804, Mar. 25, 2019.

Federation of State Medical Boards of the U.S., Inc., *Model Guidelines for the Use of Controlled Substances for the Treatment of Pain* (May 1998).

Federation of State Medical Boards of the U.S., Inc., *Model Policy for the Use of Controlled Substances for the Treatment of Pain* (May 2004), available at https://www.ihs.gov/painmanagement/includes/themes/newihstheme/display_objects/documents/modelpolicytreatmentpain.pdf.

Federation of State Medical Boards, *Guidelines for the Chronic Use of Opioid Analgesics* (Apr. 2017), https://www.fsmb.org/siteassets/advocacy/policies/opioid_guidelines_as_adopted_april-2017_final.pdf.

Hughes A et al. Prescription Drug Use and Misuse in the United States: Results from the 2015 National Survey on Drug Use and Health. *NSDUH DATA Review*. September 2016. Available at <https://www.samhsa.gov/data/sites/default/files/NSDUH-FFR2-2015/NSDUH-FFR2-2015.htm>.

IASP Guidelines, International Association for the Study of Pain, <https://www.iasp-pain.org/Guidelines?navItemNumber=648> (last visited May 10, 2019).

Joint Commission on Accreditation of Healthcare Organizations, *Pain Standards for 2001* (2001), https://www.jointcommission.org/assets/1/6/2001_Pain_Standards.pdf.

McKesson Corporation Board of Directors' Response to International Brotherhood of Teamsters (undated), available at <https://www.mckesson.com/documents/about-mckesson/board-response-to-teamsters/>.

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National Institutes of Health, *Defining the Prevalence of Chronic Pain in the United States* (Sept. 14, 2018), <https://nccih.nih.gov/research/results/spotlight/Prevalence-of-Chronic-Pain>.

National Institutes of Health, *Pain Management Fact Sheet* (Oct. 2010), available at [https://report.nih.gov/nihfactsheets/Pdfs/PainManagement\(NINR\).pdf](https://report.nih.gov/nihfactsheets/Pdfs/PainManagement(NINR).pdf).

O.R.C. § 4731.05.2 (1997).

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Overdose Death Rates, National Institute on Drug Abuse (Jan. 2019), <https://www.drugabuse.gov/related-topics/trends-statistics/overdose-death-rates>.

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Prescription Opioid Data, CDC, <https://www.cdc.gov/drugoverdose/data/prescribing.html> (last visited May 10, 2019).

Program Description, Drug Enforcement Administration Diversion Control Division, https://www.deadiversion.usdoj.gov/prog_dscrpt/index.html (last visited May 10, 2019).

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Schedules of Controlled Substance: Rescheduling of Hydrocodone Combination Products from Schedule III to Schedule II, 79 Fed. Reg. 49,661 (Aug. 22, 2014), *available at* https://www.deadiversion.usdoj.gov/fed_regs/rules/2014/fr0822.htm

Testimony of John Hammergren Chairman, President, and Chief Executive Officer, McKesson Corporation, before the Subcommittee on Oversight and Investigations, Committee on Energy and Commerce, United States House of Representatives, May 8, 2018, *available at* <https://docs.house.gov/meetings/IF/IF02/20180508/108260/HHRG-115-IF02-Wstate-HammergrenJ-20180508.pdf>.

Treatment Guidelines on Pain, World Health Organization, https://www.who.int/medicines/areas/quality_safety/guide_on_pain/en/ (last visited May 10, 2019).

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World Health Org., *WHO's Cancer Pain Ladder for Adults*, <https://www.who.int/cancer/palliative/painladder/en/> (last visited May 10, 2019).

Scientific Publications:

1. Management of opioid withdrawal symptoms. *Med Lett Drugs Ther.* 2018 Aug 27;60(1554):137-141.
2. Nonopioid drugs for pain. *Med Lett Drugs Ther.* 2018 Feb 12;60(1540):25-32.
3. Opioids for pain. *Med Lett Drugs Ther.* 2018 Apr 9;60(1544):57-64.

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